

REMARKS

Applicants have amended claims 24 and 25. Support for this amendment can be found throughout the specification as filed. For example, support may be found in the specification at page 21, line 25 through page 23, line 20; at page 27, line 28 through page 28, line 3; and at page 60, lines 14-29. No new matter has been added by way of amendment. Claims 24-33 will be pending upon entry of this amendment.

Priority/Support

The Examiner acknowledged Applicant's claim for domestic priority under 35 USC §120. However, the Examiner argued that "the application USSN 09/620,461 upon which priority is claimed fails to provide adequate support under 35 USC 112 for claims 24-33 of this application." Specifically, the Examiner argued that,

"insufficient support was identified for the following limitations:

- A. nucleotide sequence [...] at least 83% identical to the nucleic acid sequence of SEQ ID NO:21 (claim 24);
- B. a membrane-bound form of an isolated polypeptide (claim 25); and
- C. a competition binding assay (claim 27)."

Applicants traverse the objection. Applicants have amended claim 24 to replace the limitation "at least 83% identical to the nucleic acid sequence of SEQ ID NO:21" with the phrase "at least 95% identical to the nucleic acid sequence of SEQ ID NO:21". Applicants note that support for this limitation may be found in the priority application USSN 09/620,461 for example at page 27, line 28 through page 28, line 3.

In addition, Applicants have deleted the limitation "a membrane-bound form of an isolated polypeptide" from claim 25, thus rendering that part of the objection moot.

With respect to the limitation "a competition binding assay" in claim 27, Applicants note that support for this limitation can be found in original claim 21 of USSN 09/620,461, which recites, "wherein binding of the test compound is detected by...detection of binding using a competition binding assay."

Applicants respectfully request reconsideration and withdrawal of the objection of claims 24-33.

Objection to the Title

The Examiner objected to the title of the invention as not descriptive, and required that a new title be used that is “clearly indicative of the invention to which the claims are directed.” In addition, the Examiner suggested that Applicant avoid use of the word “novel” in the title, as patents are presumed to be novel and unobvious. Applicants have amended the title of the invention to recite, “SCREENING METHODS USING B7-H2 MOLECULES, MEMBERS OF THE B7 FAMILY”. Applicants submit that the title as amended is descriptive and clearly indicative of the invention to which the claims are directed. Applicants have also removed the word “novel” from the title, in accordance with the Examiner’s suggestion. Applicants therefore respectfully request reconsideration and withdrawal of the objection to the title.

Information Disclosure Statement

The Examiner acknowledged Applicant’s Information Disclosure Statement filed 08/20/2003, for which Applicants stated that copies of references have been provided in the priority application USSN 09/620,461. However, the Examiner stated that certain references (IDS Citation Nos. B1-B12, C1, C3-C4, C6-C12, and C14) have not been located in the file of the priority application, and invited Applicant to resubmit these references. In response to the Examiner’s invitation, Applicants submit herewith copies of these references. Applicants respectfully request consideration of these references.

Specification

The Examiner objected to the specification because it contains an embedded hyperlink and/or other form of browser-executable code, e.g. on page 24, line 28. In response to the Examiner’s objections and request, Applicants have amended the specification throughout to remove embedded hyperlinks and/or other forms of browser-executable code. Applicants respectfully request reconsideration and withdrawal of the objections to the specification.

ATCC Deposit

The Examiner rejected claims 24-33 under 35 USC 112, first paragraph, stating, “It is apparent that the plasmid deposited with ATCC as Accession Number PTA-2085 is required to practice the claimed invention. As a required element, it must be known and readily available to the public or

obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements...may be satisfied by a deposit of the cell line... ”

In addition, the Examiner pointed out that,

“Given the disclosure and the claims encompassing the instantly claimed materials in U.S. Patent No. 6,635,950; the conditions for the deposit of biological materials under 35 USC 112, first paragraph, with respect to the plasmid deposited with ATCC as Accession Number PTA-2085 appear to have been satisfied.”

The Examiner stated that Applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit, and a copy of the original affidavit filed in the parent application to complete the record of the instant application. In response, Applicants submit herewith a copy of the Statement of Biological Culture Deposit, filed September 23, 2002 in priority application USSN 09/620,261 for Accession Numbers PTA-2084 and PTA-2085. Applicants also submit a copy of the “Receipt in the Case of an Original Deposit Issued Pursuant to Rule 7.3 and Viability Statement Issued Pursuant to Rule 10.2”, and copy of the contract with the depository ATCC “To Deposit to Meet the Requirements of the Budapest Treaty on the International Recognition of the Deposit or Microorganisms for the Purposes of Patent Procedure”.

Applicants submit that the conditions for the deposit of PTA-2085 under 35 USC 112, first paragraph, have been satisfied. Applicants respectfully request reconsideration and withdrawal of the rejection of claims with respect to deposit of biological materials PTA-2085 under 35 USC 112, first paragraph.

**The Rejection of Claims 24-33 under 35 USC §112, First Paragraph,
(Written Description), Should Be Withdrawn**

The Examiner rejected claims 24-33 under 35 USC §112, first paragraph, as failing to comply with the written description requirement. The Examiner argued that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner stated that:

“the specification does not appear to provide an adequate written description of the following limitations:

- A. nucleotide sequence [...] at least 83% identical to the nucleic acid sequence of SEQ ID NO:21 (claim 24); and
- B. a membrane-bound form of an isolated polypeptide (claim 25);

The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the New Matter in the response to this Office Action. Alternatively, Applicant is invited to clearly point out the written support for the instant limitations."

Applicants respectfully traverse the rejection for the following reasons:

Applicants have amended claim 24 to replace the limitation "at least 83% identical to the nucleic acid sequence of SEQ ID NO:21" with the phrase "at least 95% identical to the nucleic acid sequence of SEQ ID NO:21". Applicants note that support for this limitation may be found in USSN 09/620,461 for example at page 27, line 28 through page 28, line 3.

In addition, Applicants have deleted the limitation "a membrane-bound form of an isolated polypeptide" from claim 25, thus rendering that part of the rejection moot.

With respect to the limitation "a competition binding assay" in claim 27, Applicants note that that support for this limitation can be found in original claim 21 of USSN 09/620,461, which recites, "wherein binding of the test compound is detected by...detection of binding using a competition binding assay."

Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. §112, first paragraph rejection over claims 1-4, 8, 14, and 20-25.

**The Rejection of Claims 24-33 under 35 USC §112, First Paragraph,
(Enablement), Should Be Withdrawn**

The Examiner rejected claims 24-33 under 35 USC §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Specifically, the Examiner stated, that

"The specification does not provide a sufficient enabling description of a method for identifying a compound which binds to:

- A. a polypeptide comprising an amino acid sequence which is at least 85% identical to SEQ ID NO:4;
- B. a polypeptide encoded by the nucleotide sequence which is at least 93% identical to SEQ ID NO:3; or

C. a polypeptide encoded by the nucleotide sequence which is at least 83% identical to SEQ ID NO:21.”

The Examiner argued that the

“claims recite a genus of polypeptides defined by a percent identity to a reference sequence, but do not require that the encoded polypeptides share any testable functional activity, a feature deemed essential to the instant invention...In the absence of a particular testable function and some structural basis for that function that must be maintained by members of the genus, the claimed invention is not described in such a way as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.”

Applicants respectfully traverse this rejection, however in the interest of expediting prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have amended claim 24 to recite polypeptides which comprise “an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:4, wherein the polypeptide has a B7-like co-stimulatory activity selected from the group consisting of ability to modulate T-cell proliferation, ability to modulate cytokine production, ability to up-regulate molecules that mediate cell-cell interaction, and ability to modulate antibody secretion by B-cells,” or those “encoded by a nucleotide sequence which is at least 95% identical to the nucleic acid sequence of SEQ ID NO:3 or 21, wherein the polypeptide has a B7-like co-stimulatory activity selected from the group consisting of ability to modulate T-cell proliferation, ability to modulate cytokine production, ability to up-regulate molecules that mediate cell-cell interaction, and ability to modulate antibody secretion by B-cells.”

The limitations within newly amended claim 24 are fully enabled within the specification as Applicants have provided teachings for every element needed for one of skill in the art to practice the claimed invention.

First, Applicants have provided which regions of the sequences of SEQ ID NO: 3 or 21, or those encoding SEQ ID NO:4, can be altered and still encode a polypeptide species encompassed by the claims. Specifically, Applicants have taught several domains and regions within the polypeptide of SEQ ID NO:4 which are conserved and essential for activity of the polypeptide (a B7-like protein), namely i) the signal peptide; ii) immunoglobulin V-like domain; iii) transmembrane domain; iv) four structural cysteines involved in forming disulfide bonds of the immunoglobulin domains; and v) intracellular and extracellular domains (refer to, for example, page 16, line 16 through page 17, line 23; page 18; page 21, line 4 through page 22, line 2; and Figures 9, 11 and 12). Applicants additionally provide alignments between the amino acid sequence of SEQ ID NO:4 and consensus amino acid sequences of known B7-like proteins (refer to Figures 1, 2, 6, 9 and 11), including comparison to consensus sequences (see especially Figures 9 and 11). By having identified the regions necessary for activity, Applicants have

taught which regions of the polypeptide are amenable to alterations as well as those which are not amenable to alterations.

Second, the specification teaches one how to generate functional variants by performing conservative substitutions within the polypeptide used in the claimed invention. As described in the specification, for example at page 33, line 8, a “conservative amino acid substitution” is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain.” The Applicants have also defined which of the amino acids have similar side chains, thereby providing a skilled artisan the necessary tools to generate functional variants of the polypeptide used in the claimed invention (see, for example, page 33, lines 10-23).

Finally, Applicants have provided teachings for one of skill in the art to be able to perform assays to determine whether or not specific sequences have the desired B7-like co-stimulatory activity. As taught on, for example, page 25, line 24 through page 26, line 7 of the specification, such an activity includes: ability to provide a co-stimulatory signal to T-cells; ability to bind to and modulate the function of ICOS, PD-1, CD28, CTLA-4; ability to modulate T-cell proliferation; ability to modulate cytokine production; and ability to modulate antibody secretion by B-cells. Based on these activities, one can perform assays on specific sequences to determine whether or not such sequences have the desired biological activities. Such assays include, for example, assays which monitor B7-like co-stimulatory activity set forth in the claims, e.g. “T-cell proliferation”, “modulation of cytokine production and/or release”, “up-regulation of molecules that mediate cell-cell interaction”, and “modulation of antibody secretion by B-cells”, (see, for example, page 26, line 8 through page 27, line 11; pages 62-67, especially page 64, lines 15-29). Performing such assays to determine whether or not a variant having at least 95% identity to the sequence of SEQ ID NO:4 has the desired properties would not constitute undue experimentation.

Therefore, Applicants have provided all of the necessary information to enable one of skill in the art to 1) identify regions within the polypeptide used in the claimed invention which may be altered while maintaining activity; 2) generate variants having at least 95% identity to the sequence of SEQ ID NO:4, or encoded by nucleotide sequences with at least 95% identity to the sequence of SEQ ID NO:3 or 21; and 3) perform assays to determine whether or not the sequences generated do in fact have the desired B7-like co-stimulatory activity as defined.

Therefore, contrary to the Examiner's assertions, Applicants have provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of claims 24-33. Therefore, Applicants respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. § 112, first paragraph rejection over claims 24-33.

The Rejections of Claims 24-33 under 35 USC §102(b) Should Be Withdrawn

The Examiner rejected claims 24-33 under 35 USC 102(e) as being anticipated by Coyle et al. (U.S. Patent Pub. No. 2002/0106730; 08/08/2002).

The Examiner stated that

“Coyle et al. teach and claim polypeptides identical in sequence to the instantly claimed polypeptides of SEQ ID NO:4, or encoded by a nucleic acid of SEQ ID NO:3, or deposited as ATCC No. 2085... Coyle et al. further teach and claim methods for identifying a compounds which binds to such polypeptides...”

Applicants respectfully traverse the rejection. Applicants submit that the rejection of claims under 35 USC 102 (b) as anticipated by Coyle et al. is improper because Coyle et al. is not a proper reference under 35 USC §102(b), as U.S. Patent Pub. No. 2002/0106730 is a publication of the instant application's parent application USSN 09/910,174. The present application is a continuation of USSN 09/910,174, and so is entitled to the same priority date as its parent. Therefore, Coyle et al. (U.S. Patent Pub. No. 2002/0106730) cannot be used as reference to anticipate itself in the instant application.

Applicants respectfully request reconsideration and withdrawal of the rejection of claims 24-33 under 35 USC §102(b) over Coyle et al.

Art Made of Record and Not Relied Upon

In addition, the Examiner stated that the following prior art made of record and not relied upon is considered relevant:

Venter et al. (U.S. Patent No. 6,812,339);
Mikesell et al. (U.S. Patent Pub. No. 2002/0095024); and
Freeman et al. (U.S. Patent Pub. No. 2002/0164600).

The Examiner argued that

“The references teach polypeptides which are 92.9% identical (Venter et al.) or 93.5% identical (Mikesell et al. and Freeman et al.) to the instantly claimed SEQ ID NO:4. The references also teach methods of identifying compounds which bind to such polypeptides (e.g. paragraphs 111-115 of Mikesell et al.)

Therefore, it appears that the teachings of the references anticipate the instant claimed invention (with the possible exception of claims 32 and 33). Alternatively, given the level of skill in the art at the time the invention was made, and the teachings of the

references, it appears that the instantly claimed methods would have been obvious to one of ordinary skill in the art."

Applicants respectfully traverse the rejection.

As a preliminary matter, in an effort to expedite prosecution, Applicants have amended claim 24 to recite polypeptides which comprise "an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:4, wherein the polypeptide has a B7-like co-stimulatory activity selected from the group consisting of ability to modulate T-cell proliferation, ability to modulate cytokine production, ability to up-regulate molecules that mediate cell-cell interaction, and ability to modulate antibody secretion by B-cells," or those "encoded by a nucleotide sequence which is at least 95% identical to the nucleic acid sequence of SEQ ID NO:3 or 21, wherein the polypeptide has a B7-like co-stimulatory activity selected from the group consisting of ability to modulate T-cell proliferation, ability to modulate cytokine production, ability to up-regulate molecules that mediate cell-cell interaction, and ability to modulate antibody secretion by B-cells." Thus, none of the polypeptides of Venter et al., Mikesell et al., or Freeman et al. fall under the scope of the claimed invention as amended. Therefore, none of these references anticipate the claimed invention. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 24-33 under 35 USC §102, as anticipated by Venter et al., by Mikesell et al., and by Freeman et al.

In addition, Applicants submit that the claimed invention as amended is not obvious in view of Venter et al., Mikesell et al., or Freeman et al.

Venter et al. claims priority to three U.S. provisional applications, filed on Sept. 8, Oct. 3, and Oct. 20, in the year 2000. None of these dates is earlier than the filing date of the priority application of which the instant application claims benefit, namely July 20, 2000 (U.S. Application No. 09/910,174). Therefore, Applicants submit that Venter et al. does not constitute prior art under 35 USC §102, and thus cannot be used to establish obviousness under 35 USC §103.

Furthermore, the sequences of the instantly claimed invention describe a "short" form of B7H2 protein taught in the present specification that is not disclosed or suggested in Venter et al., Mikesell et al. or Freeman et al. As described in the specification, the "B7H2 short" protein of the instant application lacks the "IgC" domain, a region of about 90 amino acids present in the "long" form, resulting in a distinct protein with a relative percent identity of 66.7% to B7H2-long (an alignment is attached as Exhibit A). None of Venter et al., Mikesell et al., or Freeman et al. discloses such a particular "short" form of B7H2 or suggests that such a particular protein would exist. Thus, one of skill in the art would neither have the motivation to search for the particular molecules of the instant invention, nor would they have an expectation of success in finding one. Therefore, one of skill in the art would not have motivation or expectation of success in arriving at the screening methods of the claimed invention as amended, which use the "B7-H2 short" protein. Applicants respectfully request reconsideration and

withdrawal of the rejection of claims 24-33 under 35 USC §103, as obvious over Venter et al., by Mikesell et al., or by Freeman et al.

CONCLUSION

In view of the amendments and remarks herein, Applicants believe that the objections and rejections presented by the Examiner are now overcome and that this application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

This paper is being filed timely, as a request for a three month extension of time is being filed concurrently herewith. It is believed no other fees are required. In the event any additional fees are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

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MILLENNIUM PHARMACEUTICALS, INC.

By


Jonathan K. Hamm
Registration No. 59,608
40 Lansdowne Street
Cambridge, MA 02139
Telephone - 617-679-7166
Facsimile - 617-551-8820